DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 333, 334, 335, 341, 344, 347, 348, 350, 355, 356, 357 and 358

[Docket No. 89N-0525]

RIN 0905-AA06

Status of Certain Over-the-Counter Drug Category II and III Ingredients

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking stating that certain ingredients in over-the-counter (OTC) drug products are not generally recognized as safe and effective or are misbranded. FDA is issuing this notice of proposed rulemaking after considering the reports and recommendations of various OTC advisory review panels and public comments on the agency's proposed regulations, which were issued in the form of a tentative final monograph (proposed rule). Based on the absence of substantive comments in opposition to the agency's proposed nonmonograph status for these ingredients as well as the failure of interested parties to submit new data or information to FDA pursuant to 21 CFR 330.10(a)(7)(iii), FDA has determined that the presence of these ingredients in an OTC drug product would result in that drug product not being generally recognized as safe and effective or would result in misbranding. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposal before the Commissioner of Food and Drugs by July 16, 1990. Written comments on the agency's economic impact determination by July 16, 1990.

ADDRESSES: Written comments, objections, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-210), Food and Drug Administration, 5600 Fishers Lane, Rockville MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In various issues of the **Federal Register**, FDA has published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), advance notices of proposed rulemaking to establish monographs for specific classes of OTC drug products, together with the recommendations of the OTC advisory review panels, which were responsible for evaluating data on the active ingredients in the specific drug class(es) in each proposed monograph. Following publication of each proposed monograph, interested parties were invited to submit comments within a set time period, with an additional period of time allowed for reply comments in response to comments filed in the initial comment period.

After evaluation and consideration of the OTC advisory review panels' recommendations and the comments and reply comments received in response to the initial publication of the advance notices of proposed rulemaking, the agency's proposed regulations in the form of various tentative final monographs for specific classes of OTC drug products were published in the **Federal Register**. Interested persons were invited to file comments, objections, and/or requests for an oral hearing before the Commissioner of Food and Drugs regarding the specific proposals within a set time period. A period of 12 months was provided for the submission of new data and information regarding each specific proposed rulemaking, and 2 additional months were provided for comments on the new data to be submitted.

This proposed rulemaking encompasses all Category II and Category III ingredients for which the periods for submission of comments and new data following the publication of a notice of proposed rulemaking have closed and for which no significant comments or new data to upgrade the status of these ingredients have been submitted. In each instance, a final rule for the class of ingredients involved has not been published to date. Other ingredients in classes of drugs for which a notice of proposed rulemaking has not been published to date will be addressed in future issues of the **Federal Register**.

Under the OTC drug review administrative procedures (21 CFR 330.10(a)(7)(ii)), the Commissioner may publish a separate tentative order covering active ingredients that have been reviewed and may propose that these ingredients be excluded from an OTC drug monograph on the basis of the Commissioner's determination that they would result in a drug product not being generally recognized as safe and effective or would result in misbranding. This order may include active ingredients for which no substantial comments in opposition to the advisory panel's proposed classification and no new data and information were received pursuant to § 330.10(a)(6)(iv) (21 CFR 330.10(a)(6)(iv)). While § 330.10(a)(7)(ii) authorizes the publication of a separate tentative order immediately following the close of the comment and new data periods for an advance notice of proposed rulemaking, the Commissioner has waited in the case of these ingredients until after proposed rulemakings were published and the periods for submission of comments and new data have ended to allow for the fullest possible opportunity for public comment and receipt of new data to upgrade the status of these ingredients.

As mentioned, no substantive comments or new data were submitted to support reclassification of any of these ingredients to monograph status. Therefore, before a final rule on each respective drug category is published, the Commissioner is proposing that these ingredients be found not generally recognized as safe and effective and that any OTC drug product containing any of these ingredients not be allowed to continue to be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an approved application. FDA has elected to act on these ingredients in advance of finalization of other monograph conditions in order to expedite completion of the OTC drug review. Manufacturers are encouraged to comply voluntarily at the earliest possible date.

Table I below lists the title and docket number of the specific rulemakings containing active ingredients that are addressed in this document together with the publication dates of the advance notice of proposed rulemaking (ANPR) and the notice of proposed rulemaking (NPR), as well as the closing dates for comments and submission of new data for each rulemaking. This proposal does not constitute a reopening of the administrative record or an opportunity to submit new data to any of the specified rulemakings. Should an interested person submit a comment indicating that substantive comments or new data were previously submitted to the administrative record for any of the specified rulemakings, the agency will review the record for that rulemaking and make a determination whether the affected ingredient shall continue to be evaluated under that specified rulemaking or be included in the final rule that will issue pursuant to this proposed rule.

FDA advises that the active ingredients discussed in this document (see table II below) will not be included in the relevant final monographs because they have not been shown to be generally recognized as safe and effective for their intended use. The agency further advises that these ingredients should be eliminated from OTC drug products 6 months after the date of publication in the **Federal Register** of a final rule in this proceeding regarding their status, regardless of whether further testing is undertaken to justify future use, and regardless of whether the relevant OTC drug monographs have been finalized at that time. The OTC drug review administrative procedures provide that any new data and information submitted after the administrative record has closed following publication of a tentative final monograph (TFM) (notice of proposed rulemaking) but prior to the establishment of a final monograph will be considered by the Commissioner only after a final monograph has been published in the **Federal Register** unless the Commissioner finds that good cause has been shown that warrants earlier consideration. (See 21 CFR 330.10(a)(7)(v).)

The agency points out that publication of a final rule under this proceeding does not preclude a manufacturer's testing an ingredient. New, relevant data can be submitted to the agency at a later date as the subject of a new drug application (NDA) that may provide for prescription or OTC marketing status. (See 21 CFR part 314). As an alternative where there are adequate data establishing general recognition of safety and effectiveness, such data may be submitted in an appropriate citizen petition to amend or establish a monograph, as appropriate. (See 21 CFR 10.30.)

TABLE I.—OTC DRUG RULEMAKINGS COVERED BY THIS NOTICE

Rulemaking	Publication date	Comment closing date	New data closing date
(1) Topical Acne Drug Products (Docket No. 81N-0114):			
ANPR	March 23, 1982	July 21, 1982	N/A.
NPR	January 15, 1985	May 15, 1985	March 17, 1986.
(2) Anticaries Drug Products (Docket No. 80N-0042):			
ANPR	March 28, 1980	July 28, 1980	N/A.
NPR	September 30, 1985	November 29, 1985	December 1, 1986.
NPR (Amended-Laboratory Testing Profiles)	June 15, 1988	October 13, 1988	August 15, 1989.
(3) Antidiarrheal Drug Products (Docket No. 78N-036D):			
ANPR	March 21, 1975	July 19, 1975	N/A.
NPR	April 30, 1986	June 30, 1986	June 30, 1987.
(4) Antiperspirant Drug Products (Docket No. 78N-0064):			
ANPR	October 10, 1978	February 7, 1979	N/A.
NPR	August 20, 1982	October 19, 1982	October 20, 1983.
(5) Boil Treatment Drug Products (Docket No. 82N-0054):			
ANPR	June 29, 1982	October 27, 1982	N/A.
NPR	January 26, 1988	March 28, 1988	March 27, 1989.
(6) Corn and Callus Remover Drug Products (Docket No. 81N-0122):			
ANPR	January 5, 1982	May 5, 1982	N/A.
NPR	February 20, 1987	April 21, 1987	April 20, 1988.
(7) Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products:			
(A) Antihistamine Drug Products (Docket No. 76N-052H):			
ANPR	September 9, 1976	January 7, 1977	N/A.
NPR	January 15, 1985	May 15, 1985	March 17, 1986.
NPR (amended)	August 24, 1987	October 23, 1987	October 25, 1988.
(B) Nasal Decongestant Drug Products (Docket No. 76N-052N):			
ANPR	September 9, 1976	January 7, 1977	N/A.
NPR	January 15, 1985	May 15, 1985	March 17, 1986.
(8) Dandruff, Seborrheic Dermatitis, and Psoriasis Drug Products (Docket No. 82N-0214):			
ANPR	December 3, 1982	May 4, 1983	N/A.
NPR	July 30, 1986	September 29, 1986	September 30, 1987.
(9) Digestive Aid Drug Products (Docket No. 81N-0106):			
ANPR	January 5, 1982	July 5, 1982	N/A.
NPR	January 29, 1988	March 29, 1988	March 29, 1989.
(10) Exocrine Pancreatic Insufficiency Drug Products (Docket No. 79N-0379):			
ANPR	December 21, 1979	May 21, 1980	N/A.
NPR	November 8, 1985	January 7, 1986	January 8, 1987.
(11) External Analgesic Drug Products:			
(A) Analgesic and Anesthetic Drug Products (Docket No. 78N-0301):			
ANPR	December 4, 1979	April 3, 1980	N/A.
NPR	February 8, 1983	April 11, 1983	April 9, 1984.
(B) Male Genital Desensitizer Drug Products (Docket No. 78N-0301):			
ANPR	September 7, 1982	January 5, 1983	N/A.
NPR	October 2, 1985	December 2, 1985	December 2, 1986.
(12) Ingrown Toenail Relief Drug Products (Docket No. 80N-0348):			
ANPR	October 17, 1980	February 16, 1981	N/A.
NPR	September 3, 1982	November 2, 1982	November 3, 1983.
(13) Laxative Drug Products (Docket No. 78N-036L):			
ANPR	March 21, 1975	July 19, 1975	N/A.
NPR	January 15, 1985	May 15, 1985	March 17, 1986.
NPR (amended—bulk laxatives)	October 1, 1986	December 1, 1986	December 1, 1987.
(14) Nailbiting and Thumbsucking Deterrent Drug Products (Docket No. 80N-0146):			
ANPR	October 17, 1980	February 16, 1981	N/A.
NPR	September 3, 1982	November 2, 1982	November 3, 1983.
(15) Oral Health Care Drug Products (Docket No. 81N-0033):			
ANPR	May 25, 1982	September 22, 1982	N/A.
NPR (nonantimicrobial ingredients)	January 27, 1988	May 26, 1988	March 27, 1989.

TABLE I.—OTC DRUG RULEMAKINGS COVERED BY THIS NOTICE—Continued

Rulemaking	Publication date	Comment closing date	New data closing date
(16) Topical Otic Drug Products for the Prevention of Swimmer's Ear (Docket No. 77N-334S):			
ANPR	December 16, 1977	April 14, 1978	N/A.
NPR	July 30, 1986	September 29, 1986	September 30, 1987.
(17) Poison Treatment Drug Products (Docket No. 81N-0050):			
ANPR	March 21, 1975	July 19, 1985	N/A.
NPR	September 5, 1978	October 5, 1978	N/A.
NPR (reproposal)	January 15, 1985	May 15, 1985	May 15, 1985.
(18) Skin Bleaching Drug Products (Docket No. 78N-0065):			
ANPR	November 3, 1978	March 5, 1979	N/A.
NPR	September 3, 1982	November 2, 1982	November 3, 1983.
(19) Skin Protectant Drug Products (Docket No. 78N-0021):			
ANPR	August 4, 1978	December 4, 1978	N/A.
NPR	February 15, 1983	April 18, 1983	April 16, 1984.
(20) Smoking Deterrent Drug Products (Docket No. 81N-0027):			
ANPR	January 5, 1982	May 5, 1982	N/A.
NPR	July 3, 1985	September 3, 1985	September 3, 1986.
(21) Wart Remover Drug Products (Docket No. 80N-0238):			
ANPR	October 3, 1980	February 2, 1981	N/A.
NRP	September 3, 1982	November 2, 1982	November 3, 1983.
NPR (amended)	March 27, 1987	May 26, 1987	May 27, 1988.

ANPR = Advance Notice of Proposed Rulemaking.
NPR = Notice of Proposed Rulemaking.
N/A = Not Applicable.

I. OTC Drug Category II and III Ingredients

Based on the criteria discussed above, FDA is proposing that the following ingredients are not generally recognized as safe and effective and are misbranded when labeled as OTC drugs for the following uses:

TABLE II.—INGREDIENTS COVERED BY THIS NOTICE

Rulemaking	Ingredient classification	
	ANPR	NPR (TFM)
(1) Topical acne drug products		
Alcloxa	II	II
Alkyl isoquinolinium bromide.	II	II
Aluminum chlorohydrex	II	II
Aluminum hydroxide	II	II
Benzocaine	II	II
Benzoic acid	II	II
Boric acid	II	II
Calcium polysulfide	II	II
Calcium thiosulfate	II	II
Camphor	II	II
Chlorhydroxyquinoline	II	II
Chloroxylenol	II	II
Coal tar	II	II
Dibenzothiophene	II	II
Estrone	II	II
Magnesium aluminum silicate.	II	II
Magnesium sulfate	II	II
Phenol	II	II
Phenolate sodium	II	II
Phenyl salicylate	II	II
Pyrilamine maleate	II	II
Resorcinol (as single ingredient).	II	II
Resorcinol monoacetate (as single ingredient).	II	II
Sodium borate	II	II
Sodium thiosulfate	II	II

TABLE II.—INGREDIENTS COVERED BY THIS NOTICE—Continued

Rulemaking	Ingredient classification	
	ANPR	NPR (TFM)
Tetracaine hydrochloride	II	II
Vitamin E	II	II
Zinc oxide	II	II
Zinc stearate	II	II
Zinc sulfide	II	II
Povidone iodine	III	III
Salicylic acid (over 2 up to 5 percent).	III	III
Thymol	II	III
(2) Anticaries drug products		
Acidulated sodium phosphate.	II	II
Sodium carbonate	II	II
Sodium monofluorophosphate (6% rinse).	II	II
Sodium phosphate	II	II
Hydrogen fluoride	N/A	III
(3) Antidiarrheal drug products		
Glycine	II	II
Scopolamine hydrobromide.	II	II
Aluminum hydroxide	III	III
Atropine sulfate	III	III
Calcium carbonate	III	III
Carboxymethylcellulose	III	III
Homatropine methylbromide.	III	III
Hyoscyamine sulfate	III	III
Lactobacillus acidophilus	III	III
Lactobacillus bulgaricus	III	III
Opium, powdered	I	III
Opium tincture	I	III
Paregoric	I	III
Phenyl salicylate	III	III
Zinc phenolsulfonate	III	III
(4) Antiperspirant drug products		
Aluminum bromohydrate	II	II
Aluminum chloride (alcoholic solutions).	II	II
Alum, potassium	III	III

TABLE II.—INGREDIENTS COVERED BY THIS NOTICE—Continued

Rulemaking	Ingredient classification	
	ANPR	NPR (TFM)
Aluminum chloride (aqueous solution) (aerosol only).	III	III
Aluminum sulfate	III	III
Aluminum sulfate, buffered (aerosol only).	III	III
Sodium aluminum chlorohydroxy lactate.	III	III
(5) Boil treatment drug products		
Aminacrine hydrochloride	II	II
Bismuth subnitrate	II	II
Calomel	II	II
Cholesterol	II	II
Ergot fluidextract	II	II
Hexachlorophene	II	II
Ichthamol	II	II
Isobutamben	II	II
Lanolin	II	II
Menthol	II	II
Methyl salicylate	II	II
Oxyquinoline sulfate	II	II
Petrolatum	II	II
Pine tar	II	II
Rosin	II	II
Rosin cerate	II	II
Sassafras oil	II	II
Thymol	II	II
Zinc oxide	II	II
Camphor	II	III
Juniper tar	II	III
Magnesium sulfate	II	III
Phenol	II	III
Sulfur	N/A	III
(6) Corn and callus remover drug products		
Acetic acid, glacial	II	II
Allantoin	II	II
Ascorbic acid	II	II
Belladonna alkaloids	II	II
Chlorobutanol	II	II
Diperodon hydrochloride	II	II
Ichthammol	II	II

TABLE II.—INGREDIENTS COVERED BY THIS NOTICE—Continued

Rulemaking	Ingredient classification	
	ANPR	NPR (TFM)
Iodine	II	II
Methylbenzethonium	II	II
Methyl salicylate	II	II
Panthenol	II	II
Phenyl salicylate	II	II
Vitamin A	II	II
Phenoxyacetic acid	III	III
Zinc chloride	III	III
(7) Cold, cough, allergy, bronchodilator and antiasthmatic drug products		
(A) Antihistamine drug products		
Methapyrilene hydrochloride.	I	II
Methapyrilene fumarate	I	II
Thenyldiamine	III	III
(B) Nasal decongestant drug products		
Allyl isothiocyanate	II	II
Turpentine oil	II	II
Camphor (lozenge)	III	III
Creosote, beechwood (oral).	III	III
Eucalyptol (lozenge)	III	III
Eucalyptol (mouthwash)	III	III
Eucalyptus oil (lozenge)	III	III
Eucalyptus oil (mouthwash).	III	III
Menthol (mouthwash)	III	III
Peppermint oil (mouthwash).	III	III
Thenyldiamine	III	III
Thymol	III	III
Thymol (lozenge)	III	III
Thymol (mouthwash)	III	III
(8) Dandruff/seborrheic dermatitis/psoriasis drug products		
Boric acid	II	II
Colloidal oatmeal	II	II
Cresol saponated	II	II
Mercury oleate	II	II
Resorcinol	II	II
Sodium borate	II	II
Alkyl isoquinolinium	III	III
Allantoin	III	III
Benzalkonium chloride	III	III
Benzethonium chloride	III	III
Calcium undecylenate	III	III
Captan	III	III
Chloroxylenol	III	III
Ethohexadiol	III	III
Eucalyptol	III	III
Juniper tar	III	III
Lauryl isoquinolinium	III	III
Menthol	III	III
Methylbenzethonium	III	III
Methyl salicylate	III	III
Phenol	III	III
Phenolate sodium	III	III
Pine tar	III	III
Povidone-iodine	III	III
Sodium salicylate	III	III
Thymol	III	III
Undecylenic acid	III	III
(9) Digestive aid drug products		
Bismuth sodium tartrate	II	II
Cellulase	II	II
Dehydrocholic acid	II	II
Duodenal substance	II	II
Garlic, dehydrated	II	II
Glutamic acid	II	II
Homatropine	II	II

TABLE II.—INGREDIENTS COVERED BY THIS NOTICE—Continued

Rulemaking	Ingredient classification	
	ANPR	NPR (TFM)
Ox bile extract	II	II
Pancreatin	II	II
Pancrelipase	II	II
Papain	II	II
Pepsin	II	II
Sorbitol	II	II
Calcium carbonate	III	III
Dihydroxyaluminum	III	III
Hemicellulase	III	III
Magnesium hydroxide	III	III
Magnesium trisilicate	III	III
Peppermint oil	III	III
Sodium bicarbonate	III	III
Sodium citrate	III	III
(10) Exocrine pancreatic insufficiency drug products		
Hemicellulase	II	II
(11) External analgesic drug products		
(A) Analgesic and anesthetic drug products		
Chloral hydrate	II	II
Methapyrilene hydrochloride.	I	II
Aspirin	III	III
Chlorobutanol	III	III
Cyclomethycaine sulfate	III	III
Eugenol	III	III
Hexylresorcinol	III	III
Salicylamide	III	III
Thymol	III	III
(B) Counterirritant drug products		
Chloral hydrate	II	II
Eucalyptus oil	III	III
(C) Male genital desensitizer drug products		
Benzyl alcohol	II	II
Camphorated metacresol	NA	II
Ephedrine hydrochloride	II	II
(12) Ingrown toenail relief drug products		
Chloroxylenol	II	II
Urea	II	II
(13) Laxative drug products		
(A) Bulk laxatives		
Carrageenan (degraded)	II	II
Agar	III	III
Carrageenan (native)	III	III
Guar gum	III	III
(B) Saline laxative		
Tartaric acid	III	III
(C) Stool softener		
Poloxamer 188	III	III
(D) Stimulant laxatives		
Calomel	II	II
Colocynth	II	II
Elaterin resin	II	II
Gamboge	II	II
Ipomea	II	II
Jalap	II	II
Podophyllum resin	II	II
Aloin	III	III
Bile salts/acids	III	III
Calcium pantothenate	III	III
Frangula	III	III
Ox bile	III	III
Prune concentrate	III	III
Prune powder	III	III
Rhubarb, Chinese	III	III
Sodium oleate	III	III
(14) Nailbiting and thumbsucking deterrent drug products		
Denatonium benzoate	III	III

TABLE II.—INGREDIENTS COVERED BY THIS NOTICE—Continued

Rulemaking	Ingredient classification	
	ANPR	NPR (TFM)
(15) Oral health care drug products (nonantimicrobial)		
Antipyrine	II	II
Camphor	II	II
Cresol	II	II
Dibucaine	II	II
Dibucaine hydrochloride	II	II
Lidocaine	II	II
Lidocaine hydrochloride	II	II
Myrrh tincture	II	II
Pyrilamine maleate	II	II
Tetracaine	II	II
Tetracine hydrochloride	II	II
Eucalyptol	III	III
Methyl salicylate	III	III
Sorbitol	N/A	III
Sugars	N/A	III
Thymol	III	III
(16) Topical OTIC drug products for the prevention of swimmer's ear		
Acetic acid	N/A	III
Glycerin, anhydrous	N/A	III
(17) Poison treatment drug products		
Ipecac fluidextract	II	II
Ipecac tincture	II	II
Zinc sulfate	II	II
(18) Skin bleaching drug products		
Mercury, ammoniated	II	II
(19) Skin protectant drug products		
Sulfur	II	II
Tannic acid	II	II
Allantoin	III	III
Zinc acetate	III	III
(20) Smoking deterrent drug products		
Clove	II	II
Coriander	II	II
Eucalyptus oil	II	II
Ginger Jamaica	II	II
Lemon oil, terpeneless	II	II
Licorice root extract	II	II
Menthol	II	II
Methyl salicylate	II	II
Quinine ascorbate	II	II
Silver nitrate	II	II
Thymol	II	II
(21) Wart remover drug products		
Benzocaine	II	II
Camphor	II	II
Castor oil	II	II
Iodine	II	II
Menthol	II	II
Acetic acid	III	III
Acetic acid, glacial	III	III
Ascorbic acid	III	III
Calcium pantothenate	III	III

II. The Agency's Tentative Conclusions on Certain OTC Drug Category II, and III Ingredients

The agency has determined that no substantive comments or additonal data have been submitted to the OTC drug review to support any of the ingredients listed above as being generally

recognized as safe and effective for the OTC drug uses specified in the table (Table II). Based on the agency's procedural regulations (21 CFR 330.10(a)(7)(ii)), the agency has determined that these ingredients should be found to be not generally recognized as safe and effective for OTC use before a final monograph for each respective drug category is established. Accordingly, any drug product containing any of these ingredients and labeled for the OTC use identified above will be considered nonmonograph and misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352) and a new drug under section 201(p) of the act (21 U.S.C. 321(p)) for which an approved application under section 505 of the act (21 U.S.C. 355) and 21 CFR part 314 of the regulations is required for marketing. As an alternative, where there are adequate data establishing general recognition of safety and effectiveness, such data may be submitted in a citizen petition to amend the appropriate monograph to include any of the above ingredients in OTC drug products. (See 21 CFR 10.30.) Any OTC drug product containing any of the above ingredients and labeled for the use identified above initially introduced or initially delivered for introduction into interstate commerce after the effective date of a final rule in this proceeding to remove these Category II and III ingredients from the market and that is not the subject of an approved application will be in violation of sections 502 and 505 of the act (21 U.S.C. 352 and 355) and, therefore, subject to regulatory action. Further, any OTC drug product subject to the final rule that is repackaged or relabeled after the effective date of the rule would be required to be in compliance with the rule regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the rule at the earliest possible date.

The agency has examined the economic consequences of this proposed rulemaking. The agency invited public comment in the notices of proposed rulemaking listed in Table I above regarding any impact that those rulemakings would have on drug products containing the above specified OTC drug ingredients. No comments on economic impacts were received. Moreover, manufacturers of products containing these ingredients have not provided any substantive data to support their continued marketing. Accordingly the agency concludes that there is no basis for the continued marketing of these ingredients for the indications listed in Table II above. Further, there are proposed monograph ingredients which manufacturers can use to reformulate affected products. In many instances, manufacturers have already reformulated their products to include monograph ingredients. As a result of this proposal, manufacturers may need to reformulate some products prior to promulgation of the applicable final monograph. However, there will be no additional costs because reformulation will be required, in any event, when the final monograph is published.

Early finalization of the nonmonograph status of the ingredients listed in this notice will benefit both consumers and manufacturers. Consumers will benefit from the early removal from the marketplace of ingredients for which safety and effectiveness have not been established. This will result in a direct economic savings to consumers. Manufacturers will benefit from being able to use alternative ingredients that have been found to be generally recognized as safe and effective without incurring additional expense of clinical testing for these ingredients. Based on the above, the agency certifies that this proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities.

Any comments on the agency's initial determination of the economic consequences of this proposed rulemaking should be submitted by July 16, 1990. Such comments should be submitted to the Dockets Management Branch (address above) and identified with the docket number found in brackets in the heading of this document and not to the docket numbers appearing in Table I above. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Interested persons may, on or before July 16, 1990, submit to the Dockets Management Branch (address above) written comments, objections, or requests for oral hearing before the Commissioner on the proposed rulemaking. A request for an oral hearing must specify points to be covered and time requested. Written comments on the agency's economic impact determination may be submitted on or before July 16, 1990. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the appropriate docket number found in brackets in the heading of this document and not the docket numbers appearing in Table I above, and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Dated: March 31, 1990.

James S. Benson,

Acting Commissioner of Food and Drugs.

[FR Doc. 90-11357 Filed 5-15-90; 8:45 am]

BILLING CODE 4160-01-M